

Delete Ad5 base pairs 357 to 4020
Insert MLP/p53 cDNA

FIG. 1B

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Met | Pro | Pro | Lys | Thr | Pro | Arg | Lys | Thr | Ala | Ala | Thr | Ala | Ala | Ala | Ala | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
| Ala | Ala | Glu | Pro | Pro | Ala | Pro | Pro | Pro | Pro | Pro | Pro | Pro | Glu | Glu | Asp | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |
| Pro | Glu | Gln | Asp | Ser | Gly | Pro | Glu | Asp | Leu | Pro | Leu | Val | Arg | Leu | Glu | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |
| Phe | Glu | Glu | Thr | Glu | Glu | Pro | Asp | Phe | Thr | Ala | Leu | Cys | Gln | Lys | Leu | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| Lys | Ile | Pro | Asp | His | Val | Arg | Glu | Arg | Ala | Trp | Leu | Thr | Trp | Glu | Lys | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| Val | Ser | Ser | Val | Asp | Gly | Val | Leu | Gly | Gly | Tyr | Ile | Gln | Lys | Lys | Lys | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| Glu | Leu | Trp | Gly | Ile | Cys | Ile | Phe | Ile | Ala | Ala | Val | Asp | Leu | Asp | Glu | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| Met | Ser | Phe | Thr | Phe | Thr | Glu | Leu | Gln | Lys | Asn | Ile | Glu | Ile | Ser | Val | |
| | | 115 | | | | | 120 | | | | | 125 | | | | |
| His | Lys | Phe | Phe | Asn | Leu | Leu | Lys | Glu | Ile | Asp | Thr | Ser | Thr | Lys | Val | |
| | 130 | | | | | 135 | | | | | 140 | | | | | |
| Asp | Asn | Ala | Met | Ser | Arg | Leu | Leu | Lys | Lys | Tyr | Asp | Val | Leu | Phe | Ala | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| Leu | Phe | Ser | Lys | Leu | Glu | Arg | Thr | Cys | Glu | Leu | Ile | Tyr | Leu | Thr | Gln | |
| | | | | 165 | | | | | 170 | | | | | 175 | | |
| Pro | Ser | Ser | Ser | Ile | Ser | Thr | Glu | Ile | Asn | Ser | Ala | Leu | Val | Leu | Lys | |
| | | | 180 | | | | | 185 | | | | | 190 | | | |
| Val | Ser | Trp | Ile | Thr | Phe | Leu | Leu | Ala | Lys | Gly | Glu | Val | Leu | Gln | Met | |
| | | 195 | | | | | 200 | | | | | 205 | | | | |
| Glu | Asp | Asp | Leu | Val | Ile | Ser | Phe | Gln | Leu | Met | Leu | Cys | Val | Leu | Asp | |
| | 210 | | | | | 215 | | | | | 220 | | | | | |
| Tyr | Phe | Ile | Lys | Leu | Ser | Pro | Pro | Met | Leu | Leu | Lys | Glu | Pro | Tyr | Lys | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| Thr | Ala | Val | Ile | Pro | Ile | Asn | Gly | Ser | Pro | Arg | Thr | Pro | Arg | Arg | Gly | |
| | | | | 245 | | | | | 250 | | | | | 255 | | |

FIG. 2A

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Asn | Arg | Ser | Ala | Arg | Ile | Ala | Lys | Gln | Leu | Glu | Asn | Asp | Thr | Arg |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Ile | Ile | Glu | Val | Leu | Cys | Lys | Glu | His | Glu | Cys | Asn | Ile | Asp | Glu | Val |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| Lys | Asn | Val | Tyr | Phe | Lys | Asn | Phe | Ile | Pro | Phe | Met | Asn | Ser | Leu | Gly |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Leu | Val | Thr | Ser | Asn | Gly | Leu | Pro | Glu | Val | Glu | Asn | Leu | Ser | Lys | Arg |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Tyr | Glu | Glu | Ile | Tyr | Leu | Lys | Asn | Lys | Asp | Leu | Asp | Ala | Arg | Leu | Phe |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| Leu | Asp | His | Asp | Lys | Thr | Leu | Gln | Thr | Asp | Ser | Ile | Asp | Ser | Phe | Glu |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Thr | Gln | Arg | Thr | Pro | Arg | Lys | Ser | Asn | Leu | Asp | Glu | Glu | Val | Asn | Val |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Ile | Pro | Pro | His | Thr | Pro | Val | Arg | Thr | Val | Met | Asn | Thr | Ile | Gln | Gln |
| | 370 | | | | | 375 | | | | | 380 | | | | |
| Leu | Met | Met | Ile | Leu | Asn | Ser | Ala | Ser | Asp | Gln | Pro | Ser | Glu | Asn | Leu |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Ile | Ser | Tyr | Phe | Asn | Asn | Cys | Thr | Val | Asn | Pro | Lys | Glu | Ser | Ile | Leu |
| | | | | 405 | | | | | 410 | | | | | 415 | |
| Lys | Arg | Val | Lys | Asp | Ile | Gly | Tyr | Ile | Phe | Lys | Glu | Lys | Phe | Ala | Lys |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Ala | Val | Gly | Gln | Gly | Cys | Val | Glu | Ile | Gly | Ser | Gln | Arg | Tyr | Lys | Leu |
| | | 435 | | | | | 440 | | | | | 445 | | | |
| Gly | Val | Arg | Leu | Tyr | Tyr | Arg | Val | Met | Glu | Ser | Met | Leu | Lys | Ser | Glu |
| | 450 | | | | | 455 | | | | | 460 | | | | |
| Glu | Glu | Arg | Leu | Ser | Ile | Gln | Asn | Phe | Ser | Lys | Leu | Leu | Asn | Asp | Asn |
| 465 | | | | | 470 | | | | | 475 | | | | | 480 |
| Ile | Phe | His | Met | Ser | Leu | Leu | Ala | Cys | Ala | Leu | Glu | Val | Val | Met | Ala |
| | | | | 485 | | | | | 490 | | | | | 495 | |
| Thr | Tyr | Ser | Arg | Ser | Thr | Ser | Gln | Asn | Leu | Asp | Ser | Gly | Thr | Asp | Leu |
| | | | 500 | | | | | 505 | | | | | 510 | | |

FIG. 2B

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Phe | Pro | Trp | Ile | Leu | Asn | Val | Leu | Asn | Leu | Lys | Ala | Phe | Asp | Phe |
| | | 515 | | | | | 520 | | | | | 525 | | | |
| Tyr | Lys | Val | Ile | Glu | Ser | Phe | Ile | Lys | Ala | Glu | Gly | Asn | Leu | Thr | Arg |
| | 530 | | | | | 535 | | | | | 540 | | | | |
| Glu | Met | Ile | Lys | His | Leu | Glu | Arg | Cys | Glu | His | Arg | Ile | Met | Glu | Ser |
| 545 | | | | | 550 | | | | | 555 | | | | | 560 |
| Leu | Ala | Trp | Leu | Ser | Asp | Ser | Pro | Leu | Phe | Asp | Leu | Ile | Lys | Gln | Ser |
| | | | | 565 | | | | | 570 | | | | | 575 | |
| Lys | Asp | Arg | Glu | Gly | Pro | Thr | Asp | His | Leu | Glu | Ser | Ala | Cys | Pro | Leu |
| | | | 580 | | | | | 585 | | | | | 590 | | |
| Asn | Leu | Pro | Leu | Gln | Asn | Asn | His | Thr | Ala | Ala | Asp | Met | Tyr | Leu | Ser |
| | | 595 | | | | | 600 | | | | | 605 | | | |
| Pro | Val | Arg | Ser | Pro | Lys | Lys | Lys | Gly | Ser | Thr | Thr | Arg | Val | Asn | Ser |
| | 610 | | | | | 615 | | | | | 620 | | | | |
| Thr | Ala | Asn | Ala | Glu | Thr | Gln | Ala | Thr | Ser | Ala | Phe | Gln | Thr | Gln | Lys |
| 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| Pro | Leu | Lys | Ser | Thr | Ser | Leu | Ser | Leu | Phe | Tyr | Lys | Lys | Val | Tyr | Arg |
| | | | | 645 | | | | | 650 | | | | | 655 | |
| Leu | Ala | Tyr | Leu | Arg | Leu | Asn | Thr | Leu | Cys | Glu | Arg | Leu | Leu | Ser | Glu |
| | | | 660 | | | | | 665 | | | | | 670 | | |
| His | Pro | Glu | Leu | Glu | His | Ile | Ile | Trp | Thr | Leu | Phe | Gln | His | Thr | Leu |
| | | 675 | | | | | 680 | | | | | 685 | | | |
| Gln | Asn | Glu | Tyr | Glu | Leu | Met | Arg | Asp | Arg | His | Leu | Asp | Gln | Ile | Met |
| | 690 | | | | | 695 | | | | | 700 | | | | |
| Met | Cys | Ser | Met | Tyr | Gly | Ile | Cys | Lys | Val | Lys | Asn | Ile | Asp | Leu | Lys |
| 705 | | | | | 710 | | | | | 715 | | | | | 720 |
| Phe | Lys | Ile | Ile | Val | Thr | Ala | Tyr | Lys | Asp | Leu | Pro | His | Ala | Val | Gln |
| | | | | 725 | | | | | 730 | | | | | 735 | |
| Glu | Thr | Phe | Lys | Arg | Val | Leu | Ile | Lys | Glu | Glu | Glu | Tyr | Asp | Ser | Ile |
| | | | 740 | | | | | 745 | | | | | 750 | | |
| Ile | Val | Phe | Tyr | Asn | Ser | Val | Phe | Met | Gln | Arg | Leu | Lys | Thr | Asn | Ile |
| | | 755 | | | | | 760 | | | | | 765 | | | |

FIG. 2C

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Gln | Tyr | Ala | Ser | Thr | Arg | Pro | Pro | Thr | Leu | Ser | Pro | Ile | Pro | His |
| 770 | | | | | | 775 | | | | | 780 | | | | |
| Ile | Pro | Arg | Ser | Pro | Tyr | Lys | Phe | Pro | Ser | Ser | Pro | Leu | Arg | Ile | Pro |
| 785 | | | | | 790 | | | | | 795 | | | | | 800 |
| Gly | Gly | Asn | Ile | Tyr | Ile | Ser | Pro | Leu | Lys | Ser | Pro | Tyr | Lys | Ile | Ser |
| | | | | 805 | | | | | 810 | | | | | 815 | |
| Glu | Gly | Leu | Pro | Thr | Pro | Thr | Lys | Met | Thr | Pro | Arg | Ser | Arg | Ile | Leu |
| | | | 820 | | | | | 825 | | | | | 830 | | |
| Val | Ser | Ile | Gly | Glu | Ser | Phe | Gly | Thr | Ser | Glu | Lys | Phe | Gln | Lys | Ile |
| | | 835 | | | | | 840 | | | | | 845 | | | |
| Asn | Gln | Met | Val | Cys | Asn | Ser | Asp | Arg | Val | Leu | Lys | Arg | Ser | Ala | Glu |
| | 850 | | | | | 855 | | | | | 860 | | | | |
| Gly | Ser | Asn | Pro | Pro | Lys | Pro | Leu | Lys | Lys | Leu | Arg | Phe | Asp | Ile | Glu |
| 865 | | | | | 870 | | | | | 875 | | | | | 880 |
| Gly | Ser | Asp | Glu | Ala | Asp | Gly | Ser | Lys | His | Leu | Pro | Gly | Glu | Ser | Lys |
| | | | | 885 | | | | | 890 | | | | | 895 | |
| Phe | Gln | Gln | Lys | Leu | Ala | Glu | Met | Thr | Ser | Thr | Arg | Thr | Arg | Met | Gln |
| | | | 900 | | | | | 905 | | | | | 910 | | |
| Lys | Gln | Lys | Met | Asn | Asp | Ser | Met | Asp | Thr | Ser | Asn | Lys | Glu | Glu | Lys |
| | | 915 | | | | | 920 | | | | | 925 | | | |

FIG. 2D

| | | | | | | |
|---|-----------------|---|------------|------------|------------|-----|
| TTCCGGTTTT | TCTCAGGGGA | CGTTGAAATT | ATTTTTGTAA | CGGGAGTCGG | GAGAGGACGG | 60 |
| GGCGTGCCCC | GCGTGCGCGC | GCGTCGTCCT | CCCCGGCGCT | CCTCCACAGC | TCGCTGGCTC | 120 |
| CCGCCGCGGA | AAGGCGTC | ATG CCG CCC AAA ACC CCC CGA AAA ACG GCC GCC | 171 | | | |
| | Met | Pro Pro Lys Thr | 5 | | | |
| | 1 | | 10 | | | |
| ACC GCC GCC GCT GCC GCC GCG GAA CCC CCG GCA CCG CCG CCG CCG CCC | 219 | | | | | |
| Thr Ala Ala Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro Pro | 15 20 25 | | | | | |
| CCT CCT GAG GAG GAC CCA GAG CAG GAC AGC GGC CCG GAG GAC CTG CCT | 267 | | | | | |
| Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro | 30 35 40 | | | | | |
| CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA | 315 | | | | | |
| Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala | 45 50 55 | | | | | |
| TTA TGT CAG AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG | 363 | | | | | |
| Leu Cys Gln Lys Leu Lys Ile Pro Asp His Val Arg Glu Arg Ala Trp | 60 65 70 75 | | | | | |
| TTA ACT TGG GAG AAA GTT TCA TCT GTG GAT GGA GTA TTG GGA GGT TAT | 411 | | | | | |
| Leu Thr Trp Glu Lys Val Ser Ser Val Asp Gly Val Leu Gly Gly Tyr | 80 85 90 | | | | | |
| ATT CAA AAG AAA AAG GAA CTG TGG GGA ATC TGT ATC TTT ATT GCA GCA | 459 | | | | | |
| Ile Gln Lys Lys Lys Glu Leu Trp Gly Ile Cys Ile Phe Ile Ala Ala | 95 100 105 | | | | | |
| GTT GAC CTA GAT GAG ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC | 507 | | | | | |
| Val Asp Leu Asp Glu Met Ser Phe Thr Phe Thr Glu Leu Gln Lys Asn | 110 115 120 | | | | | |
| ATA GAA ATC AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT | 555 | | | | | |
| Ile Glu Ile Ser Val His Lys Phe Phe Asn Leu Leu Lys Glu Ile Asp | 125 130 135 | | | | | |
| ACC AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAG TAT | 603 | | | | | |
| Thr Ser Thr Lys Val Asp Asn Ala Met Ser Arg Leu Leu Lys Lys Tyr | 140 145 150 155 | | | | | |
| GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA TGT GAA CTT | 651 | | | | | |
| Asp Val Leu Phe Ala Leu Phe Ser Lys Leu Glu Arg Thr Cys Glu Leu | 160 165 170 | | | | | |
| ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT ACT GAA ATA AAT TCT | 699 | | | | | |
| Ile Tyr Leu Thr Gln Pro Ser Ser Ser Ile Ser Thr Glu Ile Asn Ser | 175 180 185 | | | | | |
| GCA TTG GTG CTA AAA GTT TCT TGG ATC ACA TTT TTA TTA GCT AAA GGG | 747 | | | | | |
| Ala Leu Val Leu Lys Val Ser Trp Ile Thr Phe Leu Leu Ala Lys Gly | 190 195 200 | | | | | |
| GAA GTA TTA CAA ATG GAA GAT GAT CTG GTG ATT TCA TTT CAG TTA ATG | 795 | | | | | |
| Glu Val Leu Gln Met Glu Asp Asp Leu Val Ile Ser Phe Gln Leu Met | 205 210 215 | | | | | |

FIG. 3A

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| CTA | TGT | GTC | CTT | GAC | TAT | TTT | ATT | AAA | CTC | TCA | CCT | CCC | ATG | TTG | CTC | 843 |
| Leu | Cys | Val | Leu | Asp | Tyr | Phe | Ile | Lys | Leu | Ser | Pro | Pro | Met | Leu | Leu | |
| 220 | | | | | 225 | | | | | 230 | | | | | 235 | |
| AAA | GAA | CCA | TAT | AAA | ACA | GCT | GTT | ATA | CCC | ATT | AAT | GGT | TCA | CCT | CGA | 891 |
| Lys | Glu | Pro | Tyr | Lys | Thr | Ala | Val | Ile | Pro | Ile | Asn | Gly | Ser | Pro | Arg | |
| | | | | 240 | | | | | 245 | | | | | 250 | | |
| ACA | CCC | AGG | CGA | GGT | CAG | AAC | AGG | AGT | GCA | CGG | ATA | GCA | AAA | CAA | CTA | 939 |
| Thr | Pro | Arg | Arg | Gly | Gln | Asn | Arg | Ser | Ala | Arg | Ile | Ala | Lys | Gln | Leu | |
| | | | 255 | | | | | 260 | | | | | 265 | | | |
| GAA | AAT | GAT | ACA | AGA | ATT | ATT | GAA | GTT | CTC | TGT | AAA | GAA | CAT | GAA | TGT | 987 |
| Glu | Asn | Asp | Thr | Arg | Ile | Ile | Glu | Val | Leu | Cys | Lys | Glu | His | Glu | Cys | |
| | 270 | | | | | | 275 | | | | | 280 | | | | |
| AAT | ATA | GAT | GAG | GTG | AAA | AAT | GTT | TAT | TTC | AAA | AAT | TTT | ATA | CCT | TTT | 1035 |
| Asn | Ile | Asp | Glu | Val | Lys | Asn | Val | Tyr | Phe | Lys | Asn | Phe | Ile | Pro | Phe | |
| | 285 | | | | | 290 | | | | | 295 | | | | | |
| ATG | AAT | TCT | CTT | GGA | CTT | GTA | ACA | TCT | AAT | GGA | CTT | CCA | GAG | GTT | GAA | 1083 |
| Met | Asn | Ser | Leu | Gly | Leu | Val | Thr | Ser | Asn | Gly | Leu | Pro | Glu | Val | Glu | |
| 300 | | | | | 305 | | | | | 310 | | | | | 315 | |
| AAT | CTT | TCT | AAA | CGA | TAC | GAA | GAA | ATT | TAT | CTT | AAA | AAT | AAA | GAT | CTA | 1131 |
| Asn | Leu | Ser | Lys | Arg | Tyr | Glu | Glu | Ile | Tyr | Leu | Lys | Asn | Lys | Asp | Leu | |
| | | | | 320 | | | | | 325 | | | | | 330 | | |
| GAT | GCA | AGA | TTA | TTT | TTG | GAT | CAT | GAT | AAA | ACT | CTT | CAG | ACT | GAT | TCT | 1179 |
| Asp | Ala | Arg | Leu | Phe | Leu | Asp | His | Asp | Lys | Thr | Leu | Gln | Thr | Asp | Ser | |
| | | | 335 | | | | | 340 | | | | | 345 | | | |
| ATA | GAC | AGT | TTT | GAA | ACA | CAG | AGA | ACA | CCA | CGA | AAA | AGT | AAC | CTT | GAT | 1227 |
| Ile | Asp | Ser | Phe | Glu | Thr | Gln | Arg | Thr | Pro | Arg | Lys | Ser | Asn | Leu | Asp | |
| | 350 | | | | | | 355 | | | | | 360 | | | | |
| GAA | GAG | GTG | AAT | GTA | ATT | CCT | CCA | CAC | ACT | CCA | GTT | AGG | ACT | GTT | ATG | 1275 |
| Glu | Glu | Val | Asn | Val | Ile | Pro | Pro | His | Thr | Pro | Val | Arg | Thr | Val | Met | |
| | 365 | | | | | 370 | | | | | 375 | | | | | |
| AAC | ACT | ATC | CAA | CAA | TTA | ATG | ATG | ATT | TTA | AAT | TCA | GCA | AGT | GAT | CAA | 1323 |
| Asn | Thr | Ile | Gln | Gln | Leu | Met | Met | Ile | Leu | Asn | Ser | Ala | Ser | Asp | Gln | |
| 380 | | | | | 385 | | | | | 390 | | | | | 395 | |
| CCT | TCA | GAA | AAT | CTG | ATT | TCC | TAT | TTT | AAC | AAC | TGC | ACA | GTG | AAT | CCA | 1371 |
| Pro | Ser | Glu | Asn | Leu | Ile | Ser | Tyr | Phe | Asn | Asn | Cys | Thr | Val | Asn | Pro | |
| | | | | 400 | | | | | 405 | | | | | 410 | | |
| AAA | GAA | AGT | ATA | CTG | AAA | AGA | GTG | AAG | GAT | ATA | GGA | TAC | ATC | TTT | AAA | 1419 |
| Lys | Glu | Ser | Ile | Leu | Lys | Arg | Val | Lys | Asp | Ile | Gly | Tyr | Ile | Phe | Lys | |
| | | | 415 | | | | | 420 | | | | | 425 | | | |
| GAG | AAA | TTT | GCT | AAA | GCT | GTG | GGA | CAG | GGT | TGT | GTC | GAA | ATT | GGA | TCA | 1467 |
| Glu | Lys | Phe | Ala | Lys | Ala | Val | Gly | Gln | Gly | Cys | Val | Glu | Ile | Gly | Ser | |
| | 430 | | | | | | 435 | | | | | 440 | | | | |
| CAG | CGA | TAC | AAA | CTT | GGA | GTT | CGC | TTG | TAT | TAC | CGA | GTA | ATG | GAA | TCC | 1515 |
| Gln | Arg | Tyr | Lys | Leu | Gly | Val | Arg | Leu | Tyr | Tyr | Arg | Val | Met | Glu | Ser | |
| | 445 | | | | | 450 | | | | | 455 | | | | | |

FIG. 3B

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| ATG | CTT | AAA | TCA | GAA | GAA | GAA | CGA | TTA | TCC | ATT | CAA | AAT | TTT | AGC | AAA | 1563 |
| Met | Leu | Lys | Ser | Glu | Glu | Glu | Arg | Leu | Ser | Ile | Gln | Asn | Phe | Ser | Lys | |
| 460 | | | | | | 465 | | | | 470 | | | | | 475 | |
| CTT | CTG | AAT | GAC | AAC | ATT | TTT | CAT | ATG | TCT | TTA | TTG | GCG | TGC | GCT | CTT | 1611 |
| Leu | Leu | Asn | Asp | Asn | Ile | Phe | His | Met | Ser | Leu | Leu | Ala | Cys | Ala | Leu | |
| | | | | 480 | | | | | 485 | | | | | 490 | | |
| GAG | GTT | GTA | ATG | GCC | ACA | TAT | AGC | AGA | AGT | ACA | TCT | CAG | AAT | CTT | GAT | 1659 |
| Glu | Val | Val | Met | Ala | Thr | Tyr | Ser | Arg | Ser | Thr | Ser | Gln | Asn | Leu | Asp | |
| | | | 495 | | | | | 500 | | | | | 505 | | | |
| TCT | GGA | ACA | GAT | TTG | TCT | TTC | CCA | TGG | ATT | CTG | AAT | GTG | CTT | AAT | TTA | 1707 |
| Ser | Gly | Thr | Asp | Leu | Ser | Phe | Pro | Trp | Ile | Leu | Asn | Val | Leu | Asn | Leu | |
| | | 510 | | | | | 515 | | | | | 520 | | | | |
| AAA | GCC | TTT | GAT | TTT | TAC | AAA | GTG | ATC | GAA | AGT | TTT | ATC | AAA | GCA | GAA | 1755 |
| Lys | Ala | Phe | Asp | Phe | Tyr | Lys | Val | Ile | Glu | Ser | Phe | Ile | Lys | Ala | Glu | |
| | 525 | | | | | 530 | | | | | 535 | | | | | |
| GGC | AAC | TTG | ACA | AGA | GAA | ATG | ATA | AAA | CAT | TTA | GAA | CGA | TGT | GAA | CAT | 1803 |
| Gly | Asn | Leu | Thr | Arg | Glu | Met | Ile | Lys | His | Leu | Glu | Arg | Cys | Glu | His | |
| 540 | | | | | 545 | | | | | 550 | | | | | 555 | |
| CGA | ATC | ATG | GAA | TCC | CTT | GCA | TGG | CTC | TCA | GAT | TCA | CCT | TTA | TTT | GAT | 1851 |
| Arg | Ile | Met | Glu | Ser | Leu | Ala | Trp | Leu | Ser | Asp | Ser | Pro | Leu | Phe | Asp | |
| | | | | 560 | | | | | 565 | | | | | | 570 | |
| CTT | ATT | AAA | CAA | TCA | AAG | GAC | CGA | GAA | GGA | CCA | ACT | GAT | CAC | CTT | GAA | 1899 |
| Leu | Ile | Lys | Gln | Ser | Lys | Asp | Arg | Glu | Gly | Pro | Thr | Asp | His | Leu | Glu | |
| | | | 575 | | | | | 580 | | | | | 585 | | | |
| TCT | GCT | TGT | CCT | CTT | AAT | CTT | CCT | CTC | CAG | AAT | AAT | CAC | ACT | GCA | GCA | 1947 |
| Ser | Ala | Cys | Pro | Leu | Asn | Leu | Pro | Leu | Gln | Asn | Asn | His | Thr | Ala | Ala | |
| | | 590 | | | | | 595 | | | | | 600 | | | | |
| GAT | ATG | TAT | CTT | TCT | CCT | GTA | AGA | TCT | CCA | AAG | AAA | AAA | GGT | TCA | ACT | 1995 |
| Asp | Met | Tyr | Leu | Ser | Pro | Val | Arg | Ser | Pro | Lys | Lys | Lys | Gly | Ser | Thr | |
| | 605 | | | | | 610 | | | | | 615 | | | | | |
| ACG | CGT | GTA | AAT | TCT | ACT | GCA | AAT | GCA | GAG | ACA | CAA | GCA | ACC | TCA | GCC | 2043 |
| Thr | Arg | Val | Asn | Ser | Thr | Ala | Asn | Ala | Glu | Thr | Gln | Ala | Thr | Ser | Ala | |
| 620 | | | | | 625 | | | | | 630 | | | | | 635 | |
| TTC | CAG | ACC | CAG | AAG | CCA | TTG | AAA | TCT | ACC | TCT | CTT | TCA | CTG | TTT | TAT | 2091 |
| Phe | Gln | Thr | Gln | Lys | Pro | Leu | Lys | Ser | Thr | Ser | Leu | Ser | Leu | Phe | Tyr | |
| | | | | 640 | | | | | 645 | | | | | 650 | | |
| AAA | AAA | GTG | TAT | CGG | CTA | GCC | TAT | CTC | CGG | CTA | AAT | ACA | CTT | TGT | GAA | 2139 |
| Lys | Lys | Val | Tyr | Arg | Leu | Ala | Tyr | Leu | Arg | Leu | Asn | Thr | | Cys | Glu | |
| | | | 655 | | | | | 660 | | | | | 665 | | | |
| CGC | CTT | CTG | TCT | GAG | CAC | CCA | GAA | TTA | GAA | CAT | ATC | ATC | TGG | ACC | CTT | 2187 |
| Arg | Leu | Leu | Ser | Glu | His | Pro | Glu | Leu | Glu | His | Ile | Ile | Trp | Thr | Leu | |
| | | 670 | | | | | 675 | | | | | 680 | | | | |
| TTC | CAG | CAC | ACC | CTG | CAG | AAT | GAG | TAT | GAA | CTC | ATG | AGA | GAC | AGG | CAT | 2235 |
| Phe | Gln | His | Thr | Leu | Gln | Asn | Glu | Tyr | Glu | Leu | Met | Arg | Asp | Arg | His | |
| | 685 | | | | | 690 | | | | | 695 | | | | | |

FIG. 3C

| | |
|---|------|
| TTG GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG AAG | 2283 |
| Leu Asp Gln Ile Met Met Cys Ser Met Tyr Gly Ile Cys Lys Val Lys | |
| 700 705 710 715 | |
| AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC AAG GAT CTT | 2331 |
| Asn Ile Asp Leu Lys Phe Lys Ile Ile Val Thr Ala Tyr Lys Asp Leu | |
| 720 725 730 | |
| CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT TTG ATC AAA GAA GAG | 2379 |
| Pro His Ala Val Gln Glu Thr Phe Lys Arg Val Leu Ile Lys Glu Glu | |
| 735 740 745 | |
| GAG TAT GAT TCT ATT ATA GTA TTC TAT AAC TCG GTC TTC ATG CAG AGA | 2427 |
| Glu Tyr Asp Ser Ile Ile Val Phe Tyr Asn Ser Val Phe Met Gln Arg | |
| 750 755 760 | |
| CTG AAA ACA AAT ATT TTG CAG TAT GCT TCC ACC AGG CCC CCT ACC TTG | 2475 |
| Leu Lys Thr Asn Ile Leu Gln Tyr Ala Ser Thr Arg Pro Pro Thr Leu | |
| 765 770 775 | |
| TCA CCA ATA CCT CAC ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA | 2523 |
| Ser Pro Ile Pro His Ile Pro Arg Ser Pro Tyr Lys Phe Pro Ser Ser | |
| 780 785 790 795 | |
| CCC TTA CGG ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT | 2571 |
| Pro Leu Arg Ile Pro Gly Gly Asn Ile Tyr Ile Ser Pro Leu Lys Ser | |
| 800 805 810 | |
| CCA TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT CCA | 2619 |
| Pro Tyr Lys Ile Ser Glu Gly Leu Pro Thr Pro Thr Lys Met Thr Pro | |
| 815 820 825 | |
| AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG ACT TCT GAG | 2667 |
| Arg Ser Arg Ile Leu Val Ser Ile Gly Glu Ser Phe Gly Thr Ser Glu | |
| 830 835 840 | |
| AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC AGC GAC CGT GTG CTC | 2715 |
| Lys Phe Gln Lys Ile Asn Gln Met Val Cys Asn Ser Asp Arg Val Leu | |
| 845 850 855 | |
| AAA AGA AGT GCT GAA GGA AGC AAC CCT CCT AAA CCA CTG AAA AAA CTA | 2763 |
| Lys Arg Ser Ala Glu Gly Ser Asn Pro Pro Lys Pro Leu Lys Lys Leu | |
| 860 865 870 875 | |
| CGC TTT GAT ATT GAA GGA TCA GAT GAA GCA GAT GGA AGT AAA CAT CTC | 2811 |
| Arg Phe Asp Ile Glu Gly Ser Asp Glu Ala Asp Gly Ser Lys His Leu | |
| 880 885 890 | |
| CCA GGA GAG TCC AAA TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT | 2859 |
| Pro Gly Glu Ser Lys Phe Gln Gln Lys Leu Ala Glu Met Thr Ser Thr | |
| 895 900 905 | |
| CGA ACA CGA ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA | 2907 |
| Arg Thr Arg Met Gln Lys Gln Lys Met Asn Asp Ser Met Asp Thr Ser | |
| 910 915 920 | |
| AAC AAG GAA GAG AAA TGAGGATCTC AGGACCTTGG TGGACACTGT GTACACCTCT | 2962 |
| Asn Lys Glu Glu Lys | |
| 925 | |

GGATTCATTG TCTCTCACAG ATGTGACTGA TAT

2995

FIG. 3D

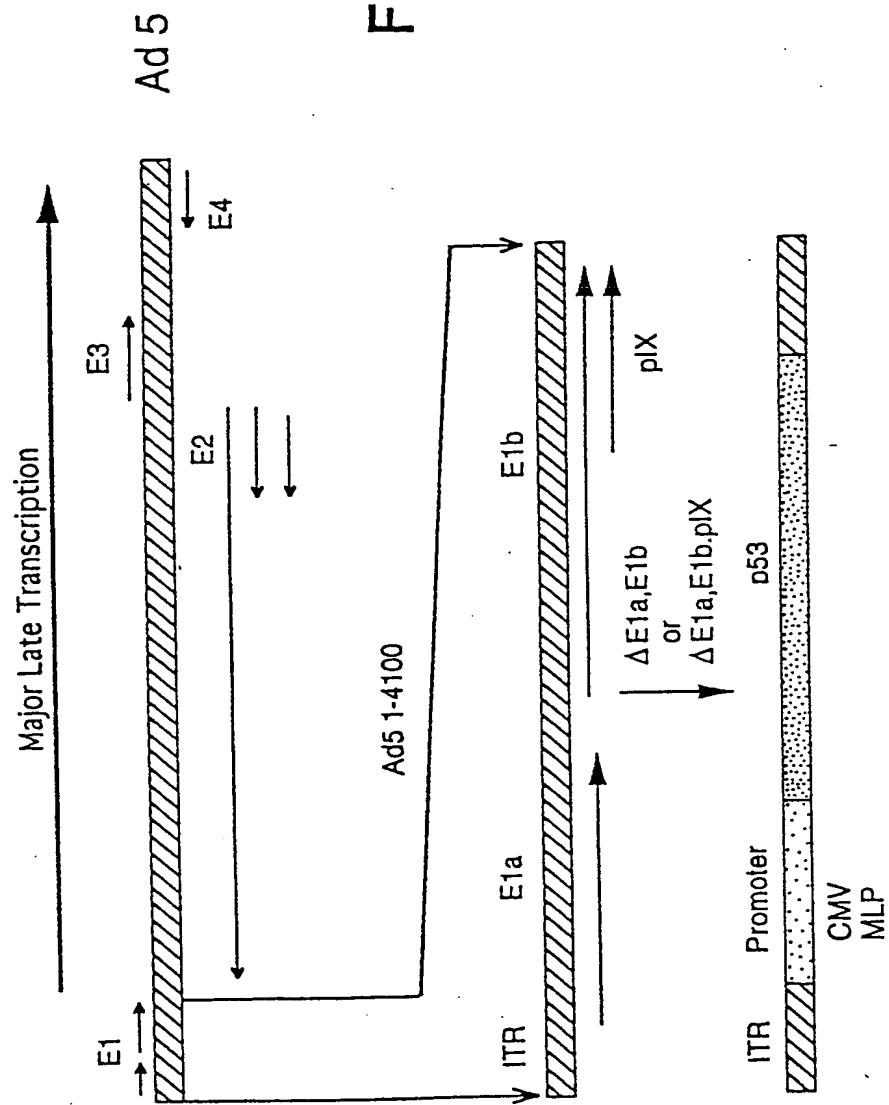


FIG. 4

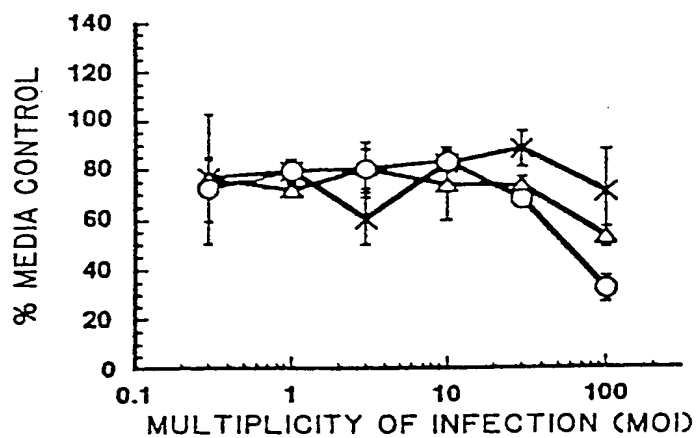


FIG. 5 A

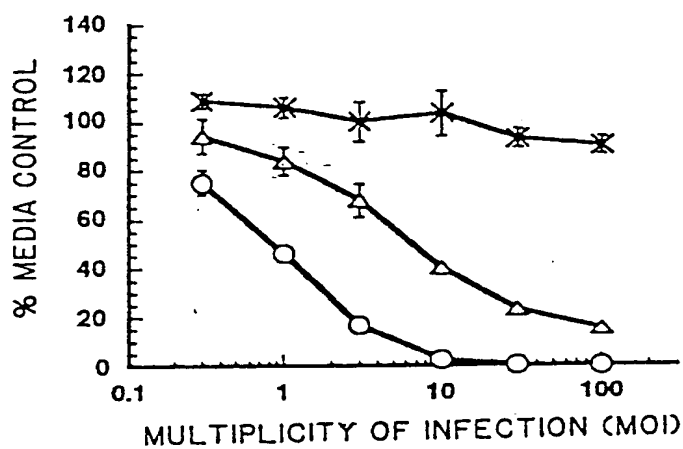


FIG. 5 B

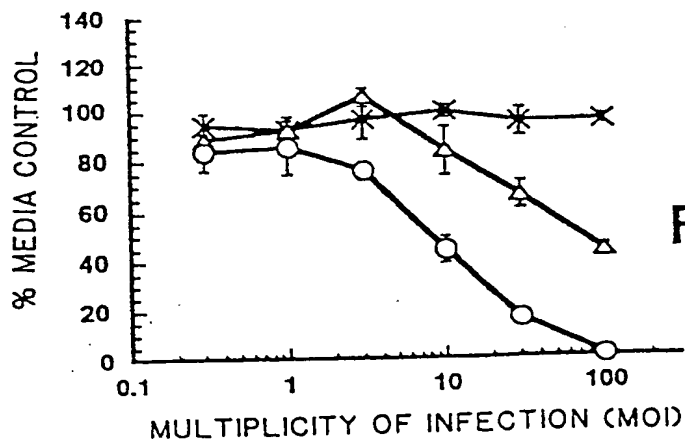
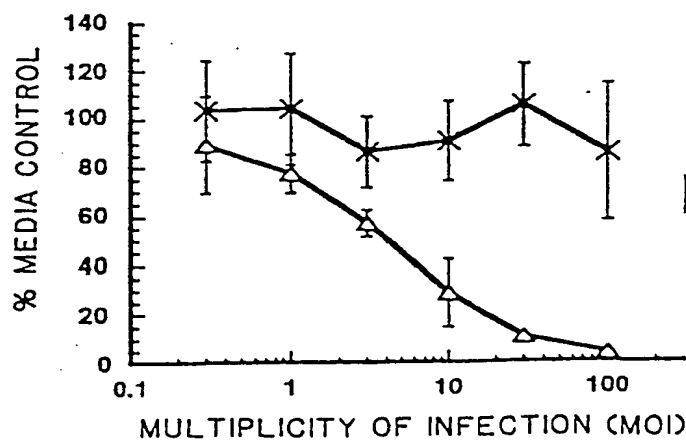
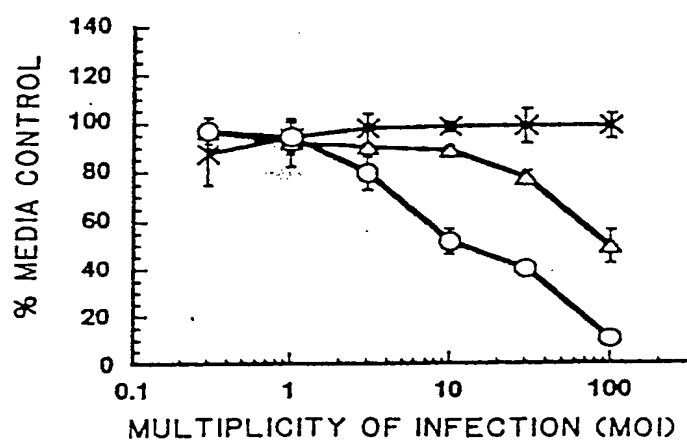
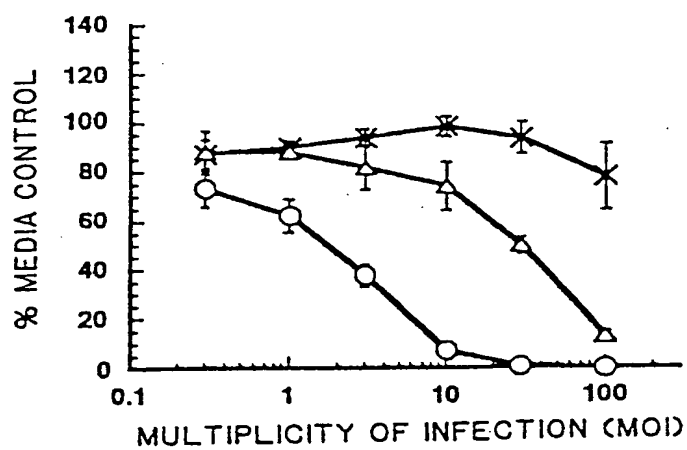
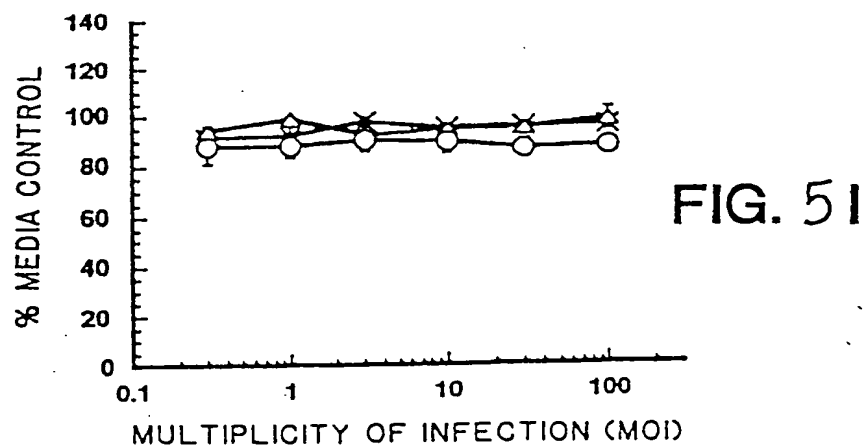
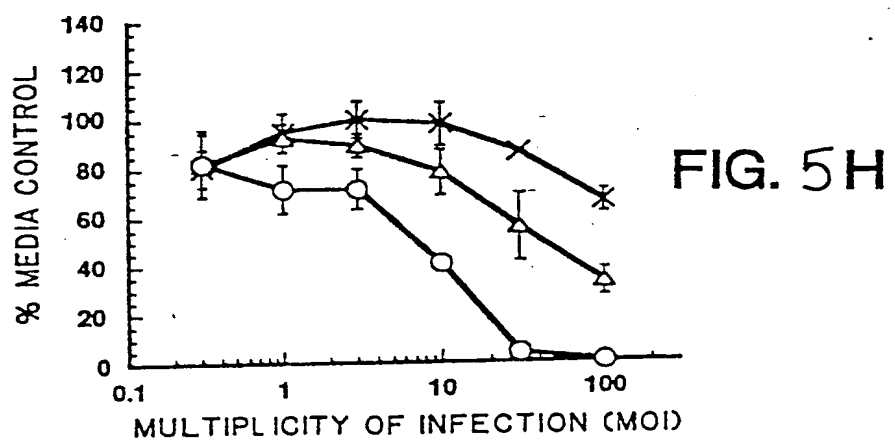
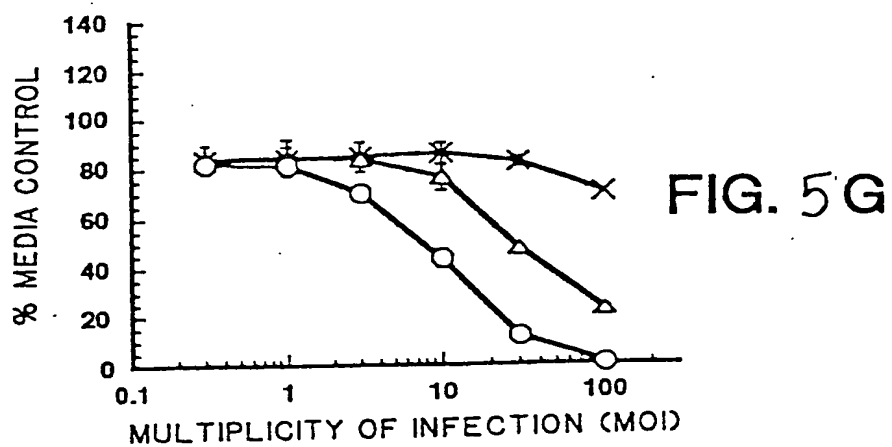


FIG. 5 C





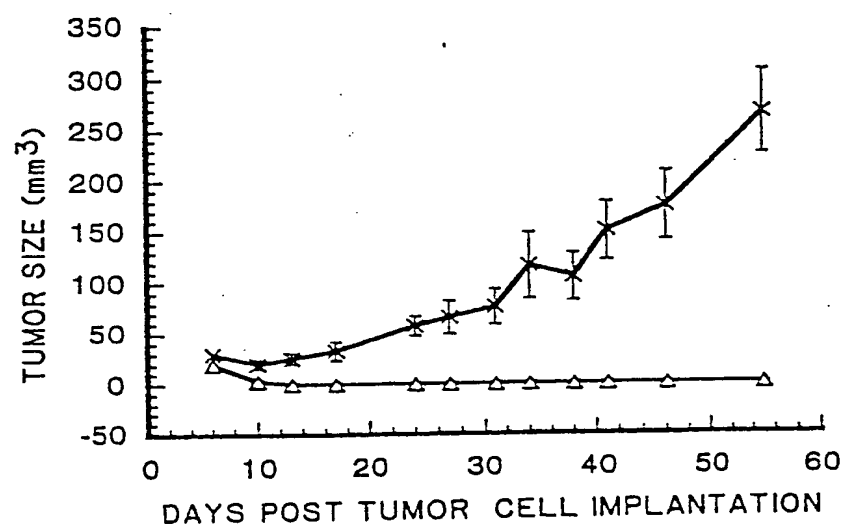


FIG. 6

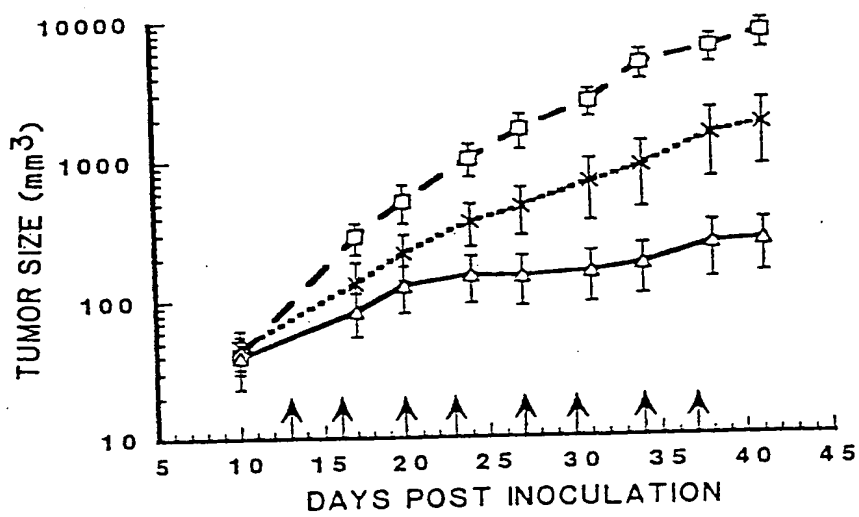


FIG. 7A

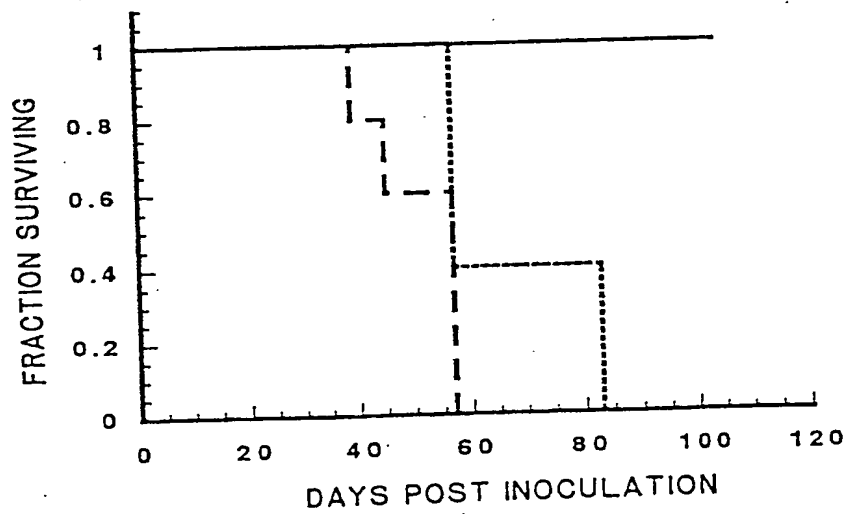


FIG. 7B

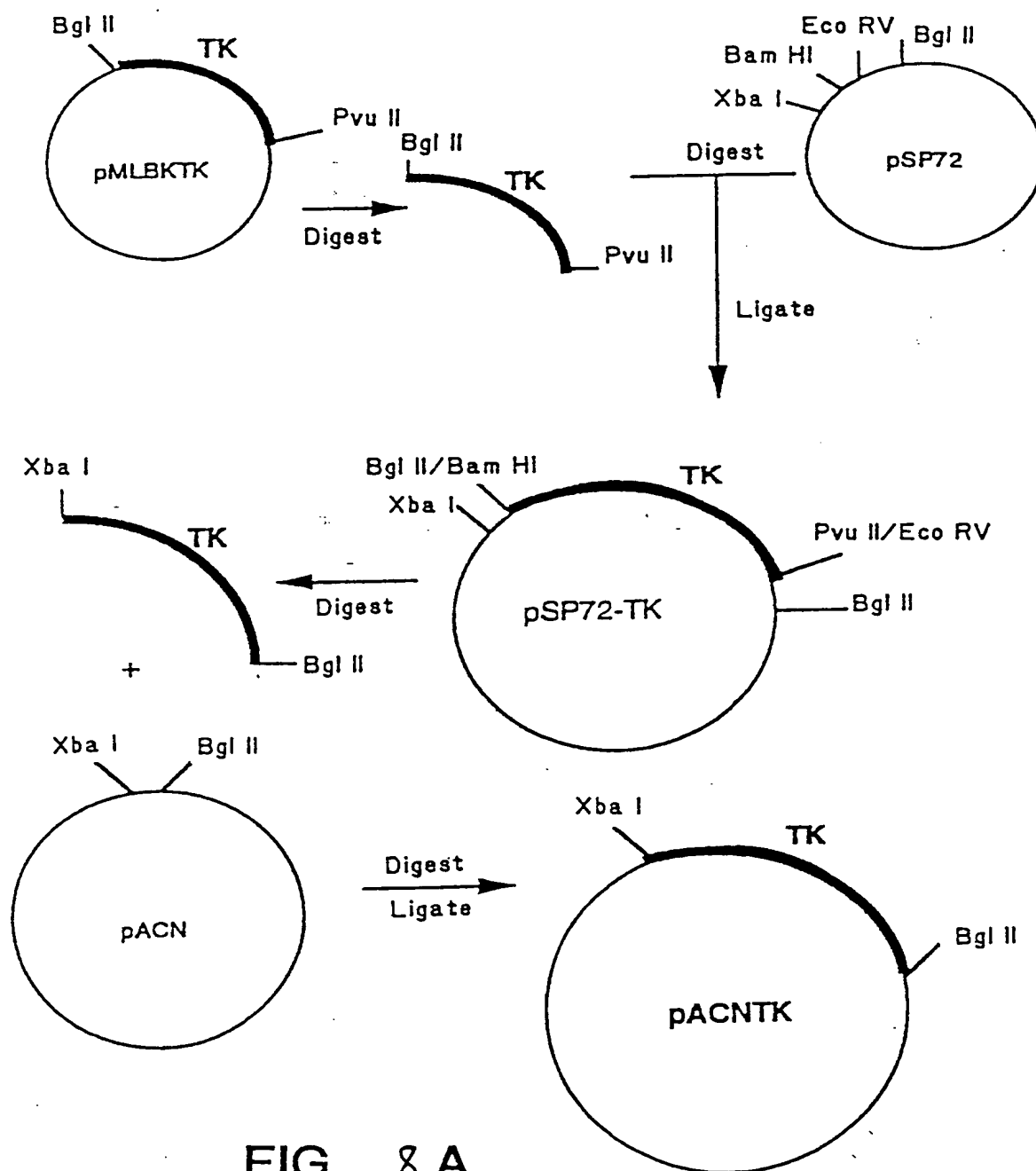


FIG. 8 A

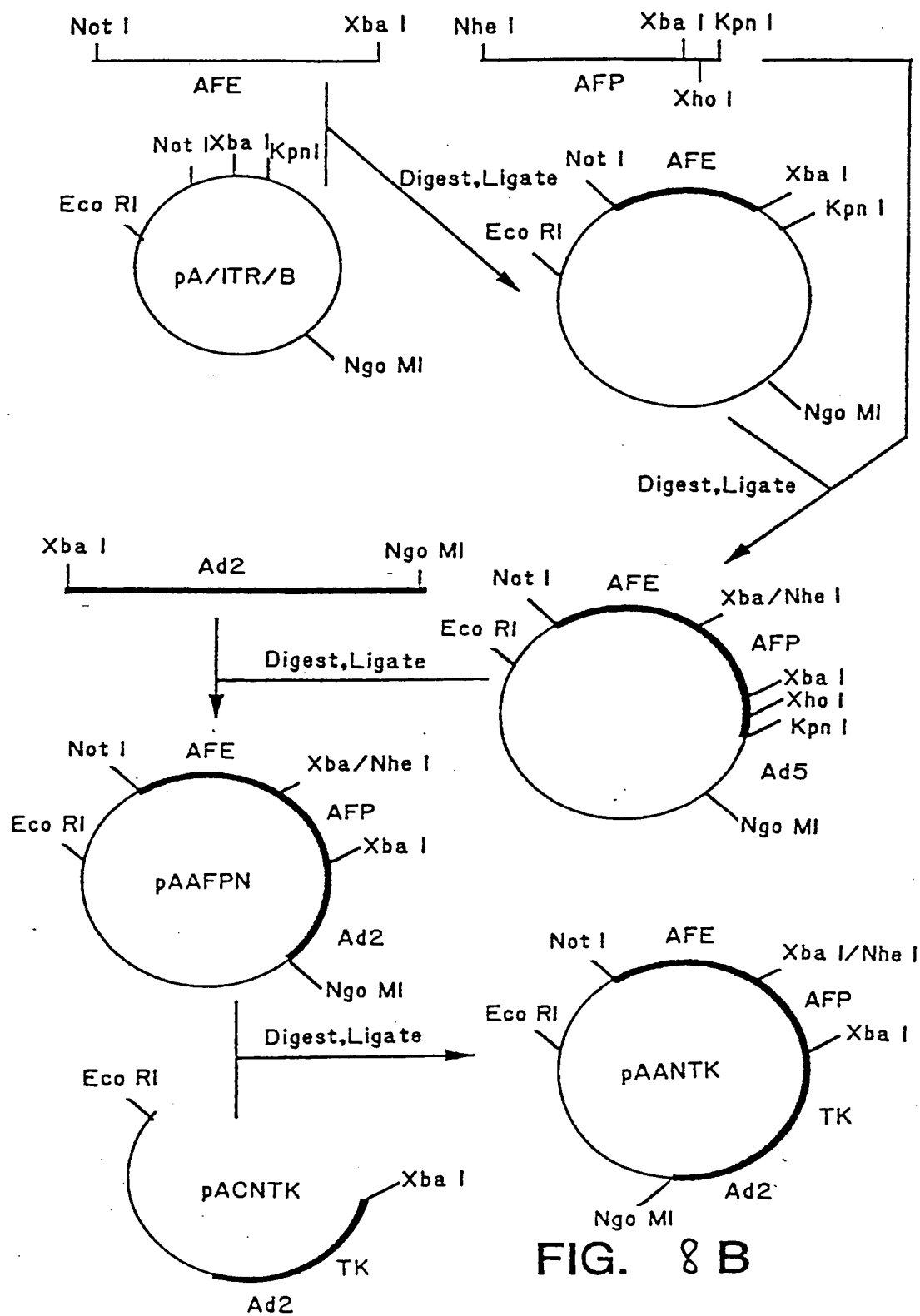


FIG. 8 B

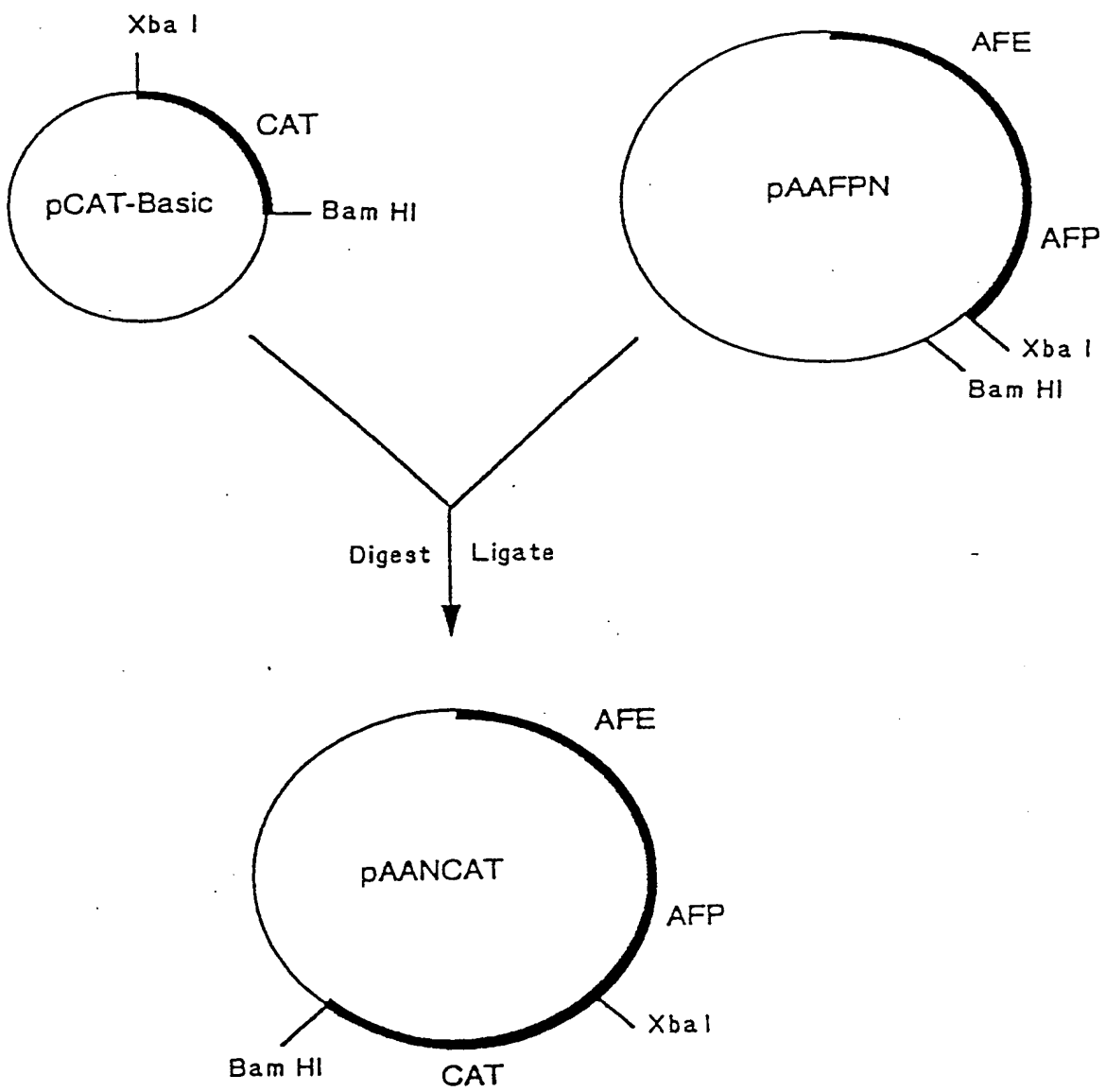


FIG. 8 C

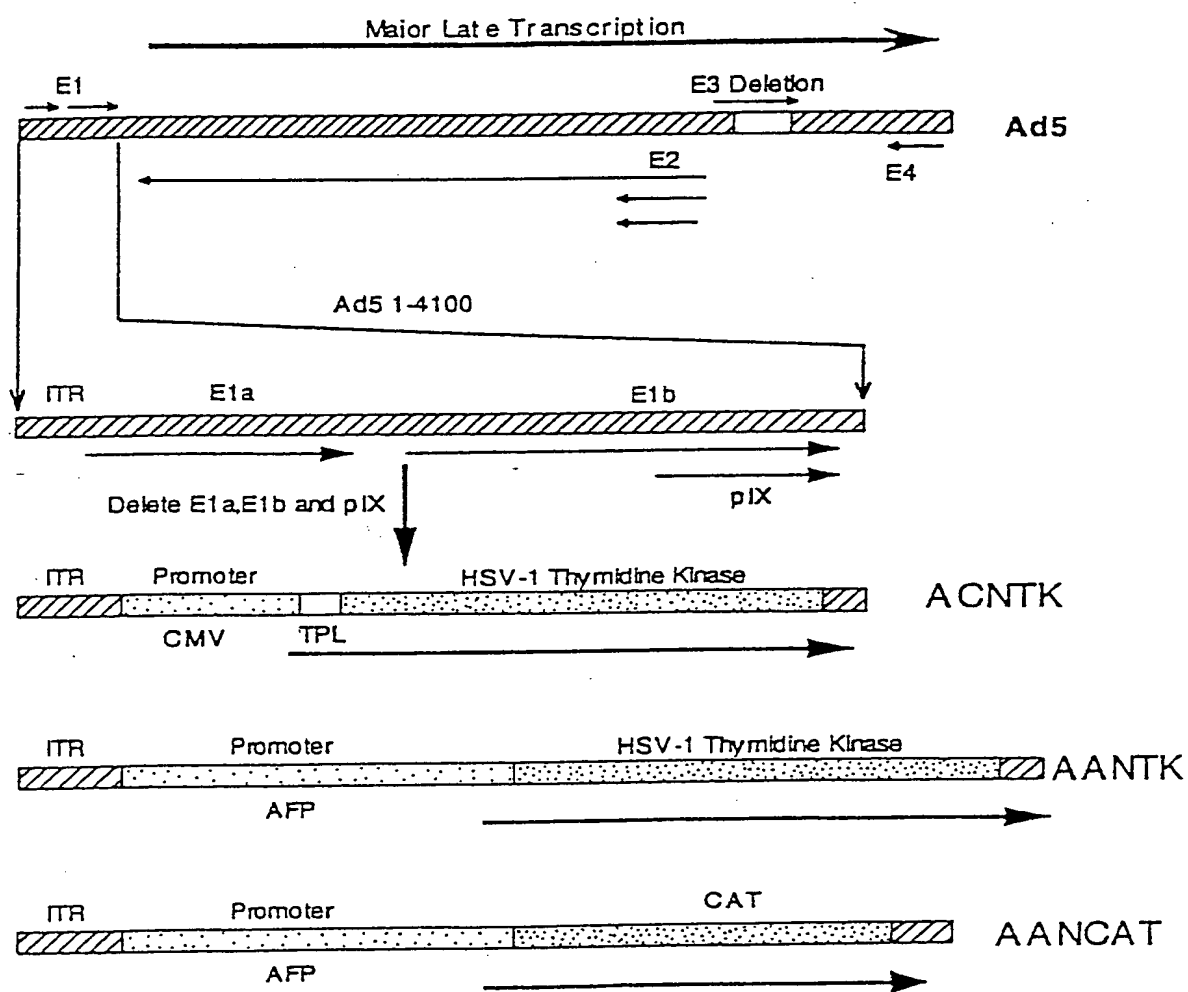


FIG. 9

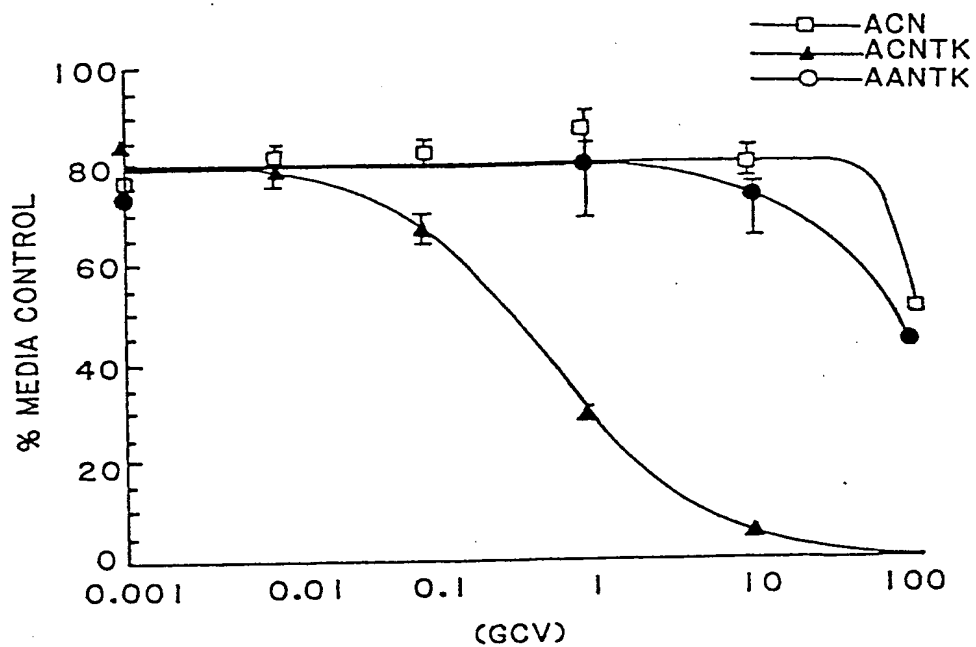


FIG. 10A

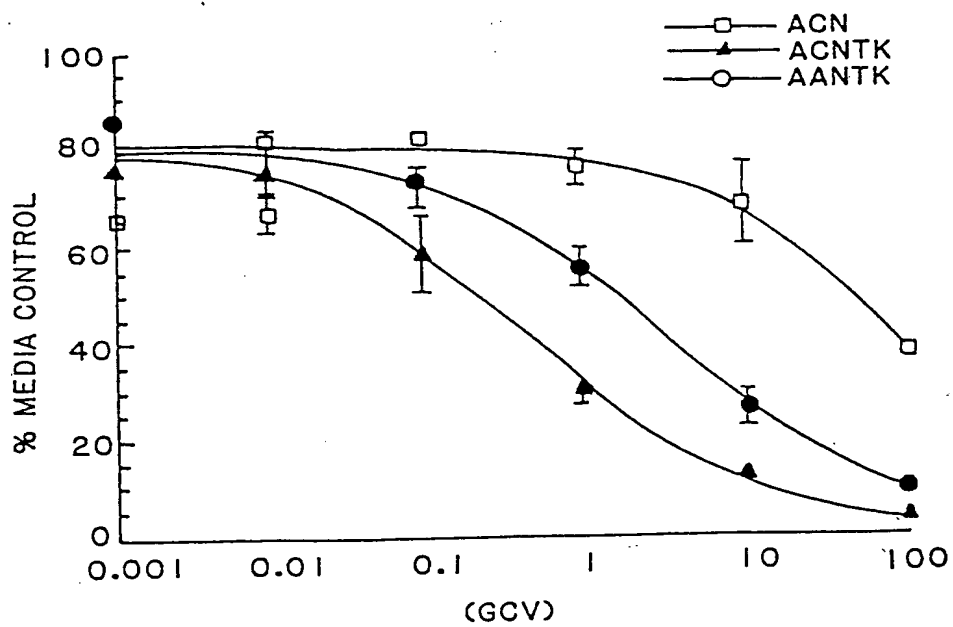


FIG. 10B

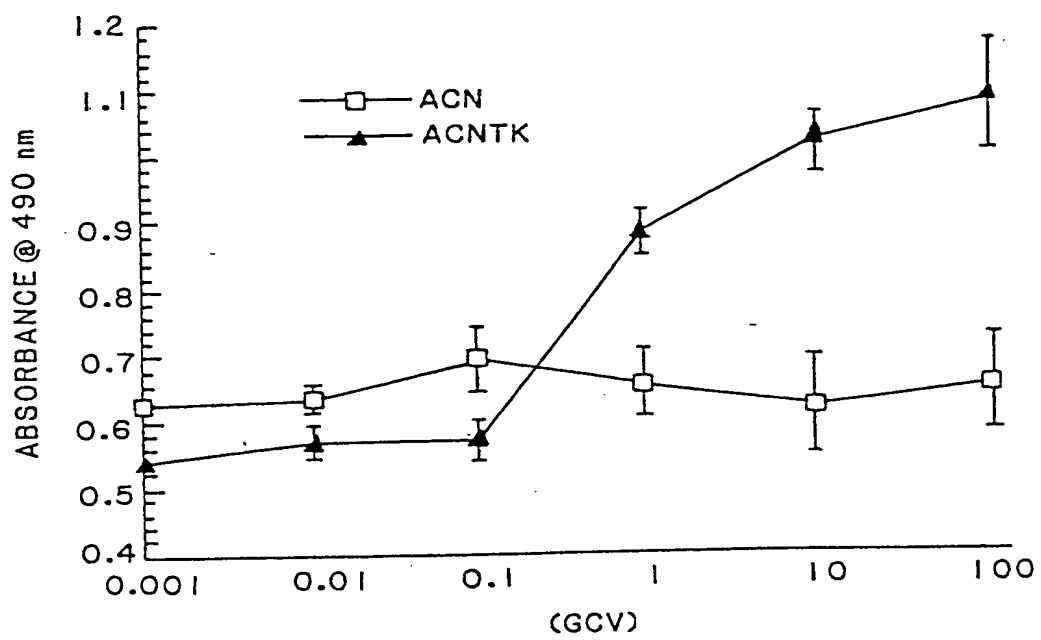


FIG. 11

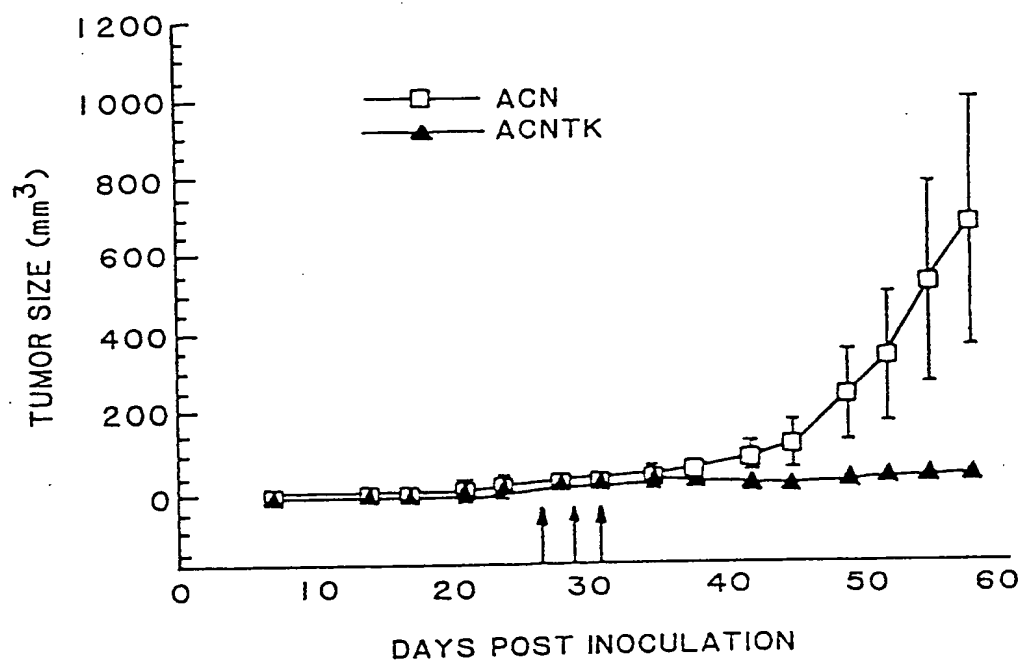


FIG. 12 A

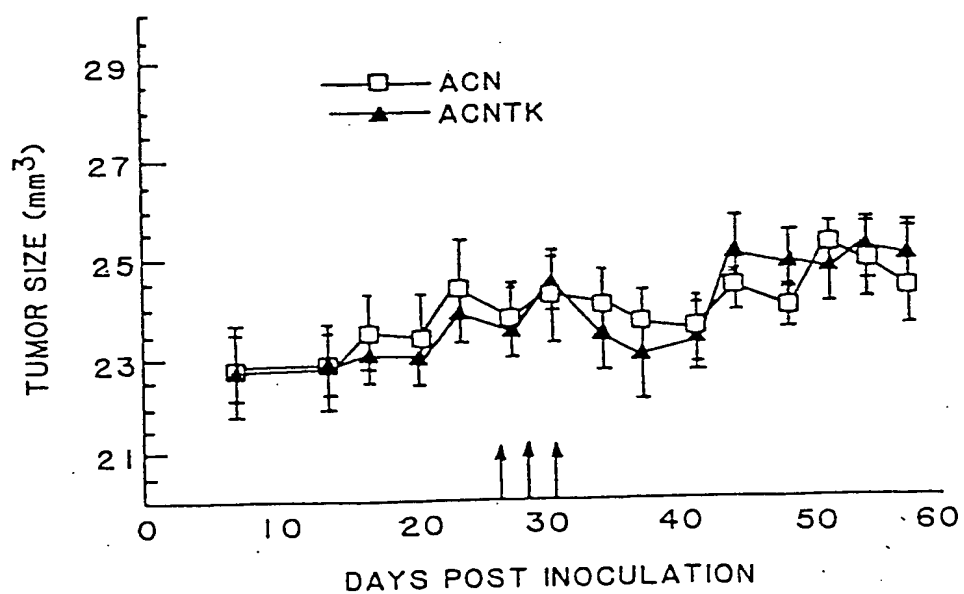


FIG. 12 B